UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/779,907	02/17/2004	Robert D. Black	9099-18	8994

20792 7590 09/20/2007

MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER	
SCHLIENTZ, LEAH H	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/779,907	BLACK ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-88 and 105-123* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-88 and 105-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 6/27/2007, in reply to the Office Action mailed 3/27/2007, is acknowledged and has been entered. Claims 43, 44, 46, 51, 70, 82 – 84, 105 and 106 have been amended. Claims 1 – 42 and 89 – 104 have been cancelled. New claims 107 – 123 have been added. Claims 43 – 88 and 105 – 123 are pending and are examined herein on the merits for patentability.

Response to Arguments

Applicant's arguments, filed 6/27/2007, with respect to the rejection of claims 70 – 76, 78 – 88 and 106 under 35 USC 112, second paragraph have been fully considered. The rejection has been withdrawn as being overcome by amendment.

Applicant's arguments, filed 6/27/2007, with respect to the rejection of claims 43, 44, 46, 47, 54 and 105 under 35 USC 102(e) as being anticipated by Shults (US 2004/0011671) have been fully considered. The rejection has been withdrawn as being overcome by amendment.

Applicant's arguments, filed 6/27/2007, with respect to the rejection of claims 43 – 45, 54 – 56, 59 – 63, 65 – 69 and 105 under 35 USC 102(b) as being anticipated by

Colvin (US 6,330,464) have been fully considered. The rejection has been withdrawn as being overcome by amendment.

Applicant's arguments, filed 6/27/2007, with respect to the rejection of claims 43 – 45, 54 – 56, 59 – 61 and 105 under 35 USC 102(e) as being anticipated by Lesho (US 2004/0054385) have been fully considered. The rejection has been withdrawn as being overcome by amendment.

Applicant's arguments, filed 6/27/2007, with respect to the rejection of the claims under 35 USC 103(a) as being unpatentable over the combined teachings of Shults, Stavridi, Colvin, Lesho and Mayinger have been fully considered. The rejections have been withdrawn as being overcome by amendment.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43 – 51, 54 – 88, 105, 106, 108 – 116 and 119 – 123 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims, as amended, recite the limitation wherein a fluorescent excitation light signal used to generate a fluorescent response of the fluorescent analyte in local tissue, with fluorescent excitation light signal having a wavelength that is at least about 400 nm in line 9 of claim 43, for example. However, such a wavelength range of "at least 400 nm" was not disclosed in the originally filed specification. The specification provides support for a sensor which generates excitation light in a wavelength range from about 400 to about 660 nm (original claim 52) or from about 400 nm to about 900 nm (p. 40, line 7). Accordingly, the limitation wherein the wavelength is "at least 400 nm" is more broad than the originally disclosed ranges. This is a new matter rejection.

Claims 43 – 88 and 105 – 116 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims, as amended, recite the limitation wherein "the fluorescent analyte is administered from a source other than the at least one sensor" in line 13 of claim 43, for example. However, such a limitation was not disclosed in the originally filed. The specification provides support for an internally administered analyte which refers to introducing an analyte or substance, systemically and/or locally, into a subject by whether ingesting the analyte,

topically applying the analyte, inhaling the analyte, and inhaling the analyate, and the like (paragraph 0057). This is a new matter rejection.

Claims 44, 45, 60 – 64 and 105 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims, as amended, recite the limitation wherein "the sensor is configured to emit excitation light into local tissue at a tumor treatment site at a depth in the local tissue that is at least 2 mm" in lines 3 – 4 of claim 44, for example. The application was examined and such a limitation of "at least 2 mm" was not found. Disclosure of specific tissue depths appear to be present in paragraph 0008, 0030, 0101, each of which specify "up to about 25 cm, and may be between about 5-25 cm, and may typically be between about 10-20 cm, below the skin of a patient..., or from about 1 cm to about 25 cm." Accordingly, there is nothing of record to demonstrate that applicant envisaged the newly claimed specific range of "at least 2 mm" at the time of filing. This is a new matter rejection.

Claims 115 and 116 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim recites the limitation wherein the "at least one sensor has a surface that is devoid of a coating having fluorescence capability and wherein the sensor detects fluorescence from the fluorescent analyte in local tissue in an uncontrolled sample volume." Applicant asserts on page 25 of the Response that support for the claims can be found in Figure 1. However, the figure and corresponding description on pages 9 – 11 of the specification do not provide support for the instantly claimed negatory proviso. With regard to a coating, the instant specification teaches that "the external surface or body of the capsule can be coated with a Parylene C material or other biocompatible coating configured so that the fluorescence excitation and response light is transmittable through the sensor wall" (paragraph 0110). This is a new matter rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 43 – 55, 60 – 63, 70 – 77 and 105 – 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black (US 2002/0102212) in view of Loeb *et al.* (US 7,096,053).

Black discloses methods of providing labeled antibodies in vivo to tissue having antigens that specifically bind a fluorescently labeled antibody. A first optical radiation is emitted into tissue to excite the labeled antibody bound to the antigen in vivo. A second optical radiation that is emitted by the excited labeled antibody in response to the excitation thereof can be detected in vivo (paragraph 0010). A platform comprising an optical radiation source which emits a first optical radiation that excites fluorescent labels. Once excited, the fluorescent labels emit a second optical radiation which may be selected to penetrate bio-fouling tissue. The optical radiation source can be a high power LED. An optical radiation detector can detect the second optical radiation through bio-fouling tissue and can be a photodiode or phototransistor. The detector can include an optical absorption filter to reduce the effects of background noise. The detector is located about 500 micrometers from the bound complexes (paragraph 0037 – 0040). The optical radiation source, detector and matrix can operate in conjunction with a processor circuit which can provide input to a telemetry system (paragraph 0053 – 0055). The in vivo system can be implanted for in vivo use whereby the ex vivo system can control operations of the system. The in vivo system can include an

indicator that provides power from the ex vivo system via an inductively powered signal from the ex vivo system. The system has a diameter of approximately 2 mm and may be cylindrical (paragraph 0056 – 0059). The package size and geometry allow for a range of coatings such as diamond like carbon or glass. Continuous monitoring of the implanted sensor is possible so that reaction kinetics can be monitored (paragraph 0062).

Black does not specifically teach that excitation light is at least 400 nm.

Loeb discloses a biosensing device for detecting biological analytes which include a biosensing element that can remain implanted for extended periods of time (abstract). Changes in fluorescence intensity and/or wavelength caused by binding of an analyte with a biosensing material, an optical fiber can transmit fluorescing evidence of the analyte from within a patient's body to an external analyzer. The system can be useful for monitoring levels of bioactive compounds that have narrow margins between safe and toxic levels (e.g. anticancer, immunosuppressive or anticoagulant drugs) or whose pharmacokinetics are uncertain. The sensing materials are based on antibodies, enzymes, etc. whose specific binding or rate of reaction depends on the concentration of analyte in adjacent fluids (column 3, lines 20+). The device comprises a light source such as a laser diode capable of producing, for example 20 mW – 24 mW. The excitation wavelength produced by the light source may be in the range of 470 – 490 nm, which is known to effectively excite certain fluorophores (column 6, lines 27+). Repeated measurements of analyte may be performed for a selected time such as at least one to three months (column 13, lines 28 – 29).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize an excitation light for causing excitation of fluor-labeled antibodies having a wavelength of at least 400 nm in the device of Black, for example, because Black teaches that the purpose of the excitation light is to excite fluor-labled antibodies, and one would have been motivated to do so because Loeb teaches the importance utilizing a wavelength which is known to excite certain fluorophores (i.e. 470 – 490 nm) for in vivo fluorescence measurements via an implantable device.

Regarding the limitations of claims 43 and 105, wherein the detection system is "for detecting fluorescence in a body of a subject associated with an administered fluorescent analyte, the fluorescent analyte including..." and wherein "the fluorescent analyte is administered from a source other than the at least one sensor, " and wherein the processor is "configured to monitor intensity over time associated with one or more of the uptake and retention of the fluorescent analyte...", it is noted that the instant claims are product claims, and the recitation of the intended use of the product has not been given patentable weight to distinguish over the cited prior art references because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). The product (detection system) claims are examined on the basis of their structural elements (i.e. a sensor, a processor, etc.), not on what type of analyte is to be detected via the detection system. Furthermore,

method steps such as "administration" are not given patentable weight in product claims.

Regarding the limitations of claims 43, 108, 112, 113, 117, 119, 121, 122 or 123 wherein the detection system is "for detecting fluorescence in a patient's body associated with an administered fluorescently labeled chemotherapeutic agent" or "for monitoring pharmacokinetics and/or pharmacodynamics" or "for determining a phenotypic response of a patient to a selected drug therapy", or the processor is "configured to monitor intensity over time associated with one or more of the uptake and retention of the fluorescent analyte..." or "configured to analyze the detected intensity over time and predict whether the subject will have a favorable response to cancer therapy," or "configured to calculate a dose of chemotherapeutic agent received at local tissue based on the intensity data over time..." or "configured to predict a bioresponse to a chemotherapeutic agent" or "configured to direct output of the excitation signal to local tissue..." and "configured to monitor fluorescence intensity of the fluorescently labeled analyte... to determine the pharmacokinetics and/or pharmacodynamics at the target site" or "configured to monitor a patient that has undergone gene therapy," or "configured to detect fluorescence to confirm micelle concentration" or "configured to monitor fluorescence intensity... and predict a phenotypic response of the patient to the therapeutic agent at the target site" it is noted that the instant claims are product claims, and the recitation of the intended use of the product has not been given patentable weight to distinguish over the cited prior art references because the intended use of the claimed invention must result in a structural difference between the claimed invention

and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). The product (detection system) claims are examined on the basis of their structural elements (i.e. a sensor and a processor). Because the cited art teaches a processor in conjunction with a sensor, any processor would be capable of being "configured" to perform the claimed intended use functions.

Regarding the limitations of claims 43, 105, 109 – 111, 117, 118 or 120, wherein the fluorescent analyte is a fluor-labeled analyte, or a fluor-labeled antibody, or a fluor-labeled chemotherapeutic agent, or is "configured to increase or decrease in response to a level or protein" it is noted that the instant claims are product claims, and the recitation of the intended use of the product has not been given patentable weight to distinguish over the cited prior art references because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). The product (detection system) claims are examined on the basis of their structural elements (i.e. a sensor, a processor, etc.), not on what type of analyte is to be detected via the detection system, because what is being detected by a device does not impose structural limitations on the device itself.

Regarding the limitation of claim 48, wherein at least one sensor is a plurality of sensors, it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Regarding the limitation the excitation light is configured to generate an excitation light that is able to penetrate light that is at least 2 mm to about 20 mm away, it is interpreted, in the absence of the contrary the excitation light of Loeb would inherently have the same properties because the same wavelength of light is used and is operated at the same power (i.e. 20 mW).

Claims 43 – 88 and 105 – 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black (US 2002/0102212) in view of Loeb *et al.* (US 7,096,053), in further view of Colvin *et al.* (US 6,330,464) and Lesho (US 2004/0054385).

Black, in view of Loeb, as set forth above, fail to disclose that the excitation light is pulsed. However, the use of pulsed excitation light in implantable fluorescence sensors is well-known in the art as shown by e.g., Colvin and Lesho.

Colvin teaches an optical-based sensor for detecting the presence of amount of an analyte (abstract). Radiation emitted from a source strikes and causes an indicator to fluoresce (column 1, lines 26 – 40). The source of radiation, such as an LED may be

powered by external means (column 2, lines 40 – 55). The capsule may include glass or epoxy resin. A plurality or radiation sensors may be used (column 24) and the LEDs can be activated for a fraction of a second, which one LED remaining off while the other is on (i.e. pulsed) and separate readings can be made due to temporal differences in emission (column 25, lines 10 – 20). The devices of Colvin also include photodiode, etc. detectors which can be present on the top, sides, etc. of the device (column 35 – 36)

Lesho teaches an implantable fluorescence sensor for detecting the concentration or presence of an analyte in the human body (paragraph 0002). The device optoelectorons circuitry, an RF oscillator, etc. for retrieving information from the sensor device and a processor for receiving and processing information signals (paragraphs 0007 – 0019). The device comprises a radiation source (e.g. LED) and a photodiode detector, and light intensity may be pulsed with a 50% duty cycle (paragraph 0074).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to provide pulsed excitation light in the devices of Black, as modified by Loeb above, because it is well known in the art that pulsed excitation light is used in similar implantable fluorescence sensors. One would have been motivated to do so because Colvin and Lesho teach that such modifications allow for e.g. separate readings for temporal differences in emission, etc. Regarding claimed limitations regarding the size of the detector in comparison with the width of the sensor body, etc. it is interpreted that such factors such as the size and positioning of detector within the

sensor body and the pulse cycle of the excitation light are elements of design of the sensor which may be variable without departing from the scope of the combined teachings of Black, Loeb, Colvin and/or Lesho because each of the cited references teach the presence of a photodiode detector and excitation light, and thus it would have been well within the skill level of the ordinary artisan to provide slight variations in such variables.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LHS

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER